Researchers develop non-invasive method to detect tumor-causing mutations in saliva

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Current methods to screen for lung cancer mutations in plasma or blood are complicated, technique-dependent and not readily available. Electric field-induced release and measurement is a reliable method to detect tumor-causing, lung cancer mutations in saliva that would be non-invasive, cost-effective and rapid. Clinicians could also use this technology to adjust their therapeutic strategies in real-time, improving clinical outcomes.

Lung cancer is the leading cause of cancer-related deaths worldwide, accounting for 27 percent of all cancer deaths among both men and women, with about 225,000 new cases diagnosed in 2014, according to the American Cancer Society. Lung cancer kills more people than colon, breast and prostate cancers combined.

Early detection improves survival rates for people diagnosed with cancer, especially people diagnosed with lung cancer. Researchers from the UCLA School of Dentistry and collaborators from several other leading research institutions have discovered that a liquid biopsy of saliva may be as successful in detecting lung cancer as testing tissue that has to be surgically removed from the lungs.

A research team, led by Dr. David Wong, the school's associate dean for research, completed a study that utilized a novel technology called electric field-induced release and measurement (EFIRM) to test lung cancer patients' saliva for epidermal growth factor receptor (EGFR) gene mutations, a sign of lung cancer, which can be treated by medication such as thymidine kinase inhibitors.

The invasive approaches traditionally used by clinicians to gather sample tissues to look for EGFR mutations have limitations, though, including difficulty obtaining a sufficient number of tumor cells, that the sample is taken from a single snapshot in time or is subject to selection bias resulting from tissue heterogeneity. These methods are also invasive, expensive and time-consuming.

In EFIRM a multiplexible electrochemical sensor uses electrode chips to enable vesicular entities in saliva called exosomes to rapidly release molecular constituents (DNA, RNA and proteins) while simultaneously detecting any mutations in tumor-causing DNA sequences. The total detection time is less than 10 minutes and required a small saliva sample.

The key finding came from a blind and randomized clinical study that used saliva samples procured from lung cancer patients. Using the EFIRM method to detect two key tumor-causing mutations in the EGFR gene (L858R and exon 19 deletion) in saliva the researchers achieved nearly identical results as with bronchoscopy-based detection of the same two mutations.

Their findings have significant implications in the quest to develop more effective, non-invasive, reliable early detection testing for lung cancer mutations. Furthermore, EFIRM testing has the potential to show how the body is reacting to cancer therapeutics and whether those therapeutics need to be adjusted to improve a patient's response.

The team was able to demonstrate that detecting EGFR mutations in saliva through the EFIRM method was just as effective as testing with plasma. Furthermore, the EFIRM method could be combined with tissue DNA testing or complement the biopsy in cases where the size of the tumors is insufficient for DNA extraction.

More information: Fang Wei, Chien-Chung Lin, Aron Joon, Ziding Feng, Gabriel Troche, Maruja E. Lira, David Chia, Mao Mao, Chung-Liang Ho, Wu-Chou Su, and David T. W. Wong "Noninvasive Saliva-based EGFR Gene Mutation Detection in Patients with Lung Cancer", *American Journal of*

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